THE TRUE ROLE OF DRUGS IN THE MANAGEMENT OF CONSUMPTIVES

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Tuberculosis is curable, or rather, if we may use the word, it is recoverable. It is never cured by the physician, but by the patient himself; that is to say, by the natural powers of recovery. These however may be, and usually need to be, stimulated, assisted and directed by wise medical guidance. Under favorable surroundings at least three-fourths of those affected with pulmonary tuberculosis should recover. Many recover spontaneously, even under unfavorable conditions.

SECONDARY ROLE OF DRUGS.

In the physician's management of consumptives—that is to say, of persons affected with pulmonary tuberculosis—drugs play a useful, but a secondary part. The principal means of treatment for the relief or recovery of these patients are included under the general term of hygienic measures; that is to say, life in the open air, with abundance of sunlight; properly selected diet and clothing; the use of water freely, both internally and externally; rest and exercise, prescribed carefully and definitely, according to the stage of the disease and the general characteristics of the patient; the use of air at modified pressures, and the like. These bring about a physiologic reinforcement of the patient's recuperative energy, and this conquers the disease.

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HYGIENIC MANAGEMENT NOW RECOGNIZED.

When I began writing on the subject of the treatment of pulmonary tuberculosis some fifteen years ago and in most of my communications on the subject since, these measures in whole or in part have been emphasized; and it is with the greatest gratification that I have observed this much neglected but ancient gospel, emphatically preached by Rush, in America, and Beddoes, in England, more than one hundred years ago, by Sydenham and others much earlier, and of which I have been an humble modern apostle, at last beginning to make itself felt, not alone in medical literature, but in contemporary practice.

THE OCCASION FOR DRUGS.

I may be pardoned, therefore, if on this occasion I speak of the use of drugs, of what may be accomplished with their aid, and of what it is useless to expect from them. Both in the general course of the disease—whether in its development toward destruction or in its progress toward recovery—and in the incidents and accidents accompanying this course, occasions arise in which the aid of drugs may usefully be sought to promote comfort, to prolong life, or to assist recovery. It is essential, however, that the physician should know definitely the powers and the limitations of the agents employed; that they should be used with definite purpose; and that their use should be sufficiently persistent while needed, but discontinued when its purpose has been accomplished.

What then are the indications for the use of drugs, and what their limitations? To answer these questions it is necessary to have a clear idea of the nature and progress of the pathologic conditions and processes embraced under the head of pulmonary tuberculosis. This is not the place to enter into detail, but certain broad outlines may be noted.

DEVELOPMENT AND PROGRESS OF PULMONARY TUBERCULOSIS. HYPOTROPHY.

In every instance of pulmonary consumption we have to deal with three distinct stages—with a fundamental or primary *(trophic)* stage, and with secondary *(bacillary)* and tertiary *(micrococcal)* stages of epi-

phenomena. The fundamental stage is a condition of lessened vital energy, lowered resistance, or malnutrition, which is not a mere vague "susceptibility," but a definite morbid state. For this, lacking a better term, we can adopt that proposed by Jaccoud, namely, "hypotrophy." I have elsewhere suggested the term "abionergy," but this involves a hypothesis not accepted by the profession or by science in general, and need not be insisted on. By whatever name we may term this state, it is not merely a general depression of function, but is accompanied with structural changes. In their intimate nature these escape our present methods of research, being probably molecular, and possibly located in the cell nuclei. When the hypotrophic status is inherited, or when it is congenital although not inherited, or when it has been acquired early in life, certain gross structural changes can sometimes be made out. Among these are especially to be noted relative deficiencies in the size of the heart and vessels and certain changes in the shape of the chest and in the physiognomy, to which attention has elsewhere been directed.[1] When it is acquired later in life these gross structural changes are not manifest.

It is in this stage that the recognition of the disease is of the highest importance and that hygienic treatment as well as roborant medication may succeed in averting the succeeding stages of destruction; but unfortunately there are no positive criteria by which it can be infallibly recognized. We can suspect, and the experienced observer can be nearly sure, that he has before him a subject of hypotrophy, but it can not be proved. The early recognition of the early tuberculization of the patient is less difficult.

SECOND OR BACILLARY STAGE. TUBERCULOSIS.

The second or bacillary stage follows the invasion of the bacillus of Koch, and is characterized by the definite histological changes giving rise to the term "tuberculosis," and by an accompanying toxemia, of which the principal symptoms are irregular fever, cough, digestive disturbance, some degree of anemia and progressive loss of strength and flesh. The physical signs

1. Consult my article on "Tuberculosis," in Vol. I. of Hare's "System of Therapeutics," Phila., 1891, pp. 724, et seq.

are now definite; slight percussion change, impairment or exaggeration of resonance with heightening of pitch, progresses to dulness perhaps just below one apex; the respiratory murmur progressively changes toward the bronchial type, cogwheel respiration being often the earliest sign; and there is progressive development, darkening and spreading of fluoroscopic shadows. Anemia of the pharyngeal and laryngeal mucous membranes is often to be observed. Sometimes the earliest overt manifestation is hemorrhage, a fortunate circumstance usually, as it leads to the prompt institution of treatment, and thus often to recovery. Cough is not infrequently absent. In this bacillary stage we have then as functional pathology, impairment of respiratory power, impairment of circulatory power, further failure of nutrition, further bacillary invasion, toxemia.

THIRD OR MICROCOCCAL STAGE. PHTHISIS. CONSUMPTION.

The third and most dangerous stage follows the invasion of various bacteria, principally belonging to the tribes of streptococci and staphylococci, for which the ground has been prepared by the destructive changes (caseation, etc.) of the preceding group of epiphenomena; those, namely, dependent on the invasion of the tubercle bacillus. Further destruction and further toxemia with hectic fever and increased emaciation, perhaps frequent hemorrhages, greater cough, progressive feebleness, sleeplessness, night sweats, diarrhea, dropsy, and the like, together with recurrent attacks of lobar and lobular pneumonia and other complications, local and general, mark the progress of phthisis toward death.

Histologically we speak of the secondary epiphenomena as the stage of infiltration; of the tertiary epiphenomena as the stage of softening or cavity-formation. Both processes may be present in different degree and extent in the same lung or in two lungs of same patient.

ACUTE AND RECURRENT TUBERCULOUS BRONCHOPNEUMONIA.

I have excluded from consideration acute disseminated or miliary tuberculosis, of which the pulmonary phenomena are but part of a general process, from which recovery is at least doubtful. Attention must be called,

however. to the group of cases of acute tuberculous bronchopneumonia, in which the secondary and tertiary groups of epiphenomena can not strictly be separated, occurring either coincidently or with but slight interval. Then, too, there is a group of cases in which destructive tertiary phenomena occur early, but in limited areas, and with but slight tendency to extension. The progress of the case is frequently interrupted by remissions or even by intermission of long duration.

COMPLEXITY OF SEMEIOLOGY.

Thus a varied and apparently contradictory semeiology arises, but analysis will always show that in some portion of the lung the secondary or tertiary phenomena predominate, and that the general symptoms depend partly on the local conditions, and partly on the predominant toxemia. There are thus minor stages or phases within the major stages.

NECESSITY FOR INDIVIDUALIZATION.

Quite obviously the treatment applicable at a given stage or phase of these complex processes differs from that applicable at any other stage, preceding or succeeding. Moreover, individual patients present great differences in their response to hygienic measures, these differences being dependent on the same constitutional powers or weaknesses that have enabled them to resist, or have made them succumb to some or all of the morbid influences. Thus each case becomes an individual study, and so continues throughout its different phases, and whatever is said concerning the general management of patients at various stages of the disease is to be understood as being thus qualified.

NO SPECIFIC.

We are now prepared to discuss the use of drugs. In the first place, it must be evident that no specific against the exciting causes of the disease or against any of the morbid processes is to be looked for. As the hygienic management of consumptives is designed to build up their vital resistance, so the auxiliary medication must have this for its primary object, incidentally combating special morbid phenomena or groups of phenomena which of themselves introduce special dangers. While I can not go so far as my friend, Dr. Mays, in looking

on consumption as a neurosis, there is little doubt that among the failures of nutrition, which prepare the ground for tuberculosis, the nervous system is involved.

NERVINES.

Drugs useful from this standpoint are arsenic, strychnin, cod-liver oil, hypophosphites and other preparations of phosphorus, among which are probably to be included the nuclein group and thymus-gland extract. Strychnin should be given at first in small doses, and according to circumstances may sometimes be increased to very large doses, though only for limited periods. Its use should not be continued indefinitely, as this tends to exhaust nervous structure and nervous energy. Cod-liver oil is a fatty food and seems to have some special suitability to the needs of the nervous structures for aliment. Whether arsenic affects the nerves directly or indirectly through its action on the blood and other tissues, I do not know; but it is to be placed in the first rank as a nerve tonic. These agents are useful in the primary stage, before the invasion of the bacillus, and in the early stages of bacillary action. Their usefulness is less apparent in the later stages, though if recession of morbid phenomena takes place in these stages they may again be used.

DIGESTANTS.

Agents to improve digestion are useful from the standpoint of general nutrition. These do not differ in principle, in method of application, or in character, from the agents used for similar purposes in other affections. Strychnin and arsenic again have application; while lavage or the drinking of hot water and the use of gastric and intestinal antiseptics, sedatives and stimulants; of phosphoric, hydrochloric and nitric acids; of digestive ferments, pepsin, pancreatin, diastase, papain and the like, must be guided by the special symptoms and responses of the individual case.

HEMATINICS.

As a rule there is very little positive anemia in the early stages of tuberculosis, but the same group of hematinic agents that are used in other anemias are applicable here. Thus again arsenic is of service; and iron,

gold and sodium chlorid, palladium chlorid, the nucleins, bone-marrow and the like also prove useful.

ELIMINANTS.

It is necessary that the skin should be kept in good condition and that all the eliminative functions should be properly performed. The daily bathing and sponging tends to keep up the tone of the peripheral vessels and of the skin, while diuretics and laxatives, of which spartein and cascara may be taken as types, are employed from time to time if indicated.

AGENTS ACTING ON THE CIRCULATION.

The condition of the circulation needs separate study, and more specially in the primary stage and in the acute manifestations of the tertiary stage. I desire therefore to call special attention to the usefulness of nitroglycerin in the early stages and of digitalis in the acute processes of the tertiary stage.

Nitroglycerin by its action in relaxing the peripheral vessels both in the systemic and pulmonary circulations, permits the work of the heart to be performed better and with less expenditure of vital energy. Vascular insufficiency is, as we have already noted, one of the characteristics of congenital hypotrophy, and the absence of blood-channels from the histological tubercle is not without significance in this connection. One of the greatest advantages of the use of the inhalation of compressed air with expiration into rarefied air, as well as one of the chief factors in the altitude cure of pulmonary tuberculosis, is the increased distribution of blood and nutrient lymph into the ultimate vascular channels and pericellular spaces. Even without the inhalation of compressed air, nitroglycerin aids such dissemination of reconstructive pabulum, as well as the better collection and excretion of waste which accompanies the improved ultimate circulation.

Digitalis was especially commended by Beddoes as the result of his empiric observation, in cases of galloping consumption, with high fever and rapid pulse, and he reported striking instances of the benefit following its use. I have no rational explanation to offer of this action, unless the inhibition of the heart may account for it, but empirically I can confirm Beddoes' observa-

tion. I have frequently seen remarkable reduction of fever and the accompanying group of hectic phenomena follow the use of large doses of digitalis, both in the late stages of chronic pulmonary tuberculosis and in the recurring acute attacks of tuberculous broncho-pneumonia, or of lobar pneumonia in tuberculous patients. It must, however, be given continuously and fearlessly, up to the point of tolerance, the only counterindication being evidences of untoward effect on the stomach. Merck's German digitalin may then be used in its place; the dose being from 1/24 to 1/8 of a grain, or even more, thrice daily.

IODIN GROUP.

Of drugs used to combat more or less directly the local and hemic results of bacillary invasion, two groups of agents have stood the test of time—the iodin group and the creosote group. The first is applicable especially in the early stages of pulmonary infiltration; the latter, when destructive changes belonging to the bacillary phenomena have begun, and also when the pyemia and increased destruction of the tertiary processes are manifest. The most useful of the iodin group is iodoform, which must be given in comparatively large doses and over large periods. The dose, however, is to be small at the beginning and to be increased very gradually to the point of tolerance. If there is any disease whatever in which it is a mistake to look for results quickly or to be in a hurry to make changes in the administration of drugs, it is the one under consideration. Chronic cases require chronic, that is to say, persistent treatment, and the organism must often be accustomed gradually to the remedy. Beginning with ½ grain of iodoform three times daily, after meals, the dose may be increased, little by little, until in the course of two or three months it reaches 5 grains, three times daily. Balsam of Peru is an excellent excipient and the addition of a digestive ferment sometimes enables it to be borne by stomachs otherwise intolerant. Iodoform may usefully be combined with iron, with arsenic, with strychnin, and with digitalis, in cases in which these latter drugs seem indicated.

A favorite formula of my own in the early stages of the bacillary disease is as follows:

℞. Iodoformi ..... gr. i-iii
Strychninæ sulphatis ..... gr. 1/40
Arsenii iodidi ..... gr. 1/12
Balsami Peruvianæ ..... gr. ii-v

Mix and encapsulate. Dose: one capsule after meals three times daily.

Sometimes ichthyol is used as the excipient, with or without the Peruvian balsam. Ichthyol has itself been recommended as of use in pulmonary tuberculosis, in doses of 5 grains or more, thrice daily. Crude or refined petroleum may be used similarly.

Flick, of Philadelphia, a careful observer and accurate reporter, states that he has seen much benefit from the inunction of iodoform in cod-liver oil or lanolin. Lately he has substituted europhen for the iodoform, on account of the disagreeable odor of the latter. For the benefit of those who prefer to use iodoform in this way, I would state that attar of rose in very minute proportion will successfully mask the odor. My own experience with the inunction method is slight, and it did not seem to possess any special advantage over the administration of the drug by the mouth. Iodoform dissolved in sterilized olive-oil, in the proportion of 1 to 10, may be given likewise by intratracheal injection, in quantities not exceeding ½ dram.

Powdered iodoform may be insufflated into the larynx, or iodoform dissolved in ether—1 to 10—be applied by sponge, especially in cases of tuberculous laryngitis, after the application of lactic acid or formalin, and the dose need not be measured especially. There is no objection to covering the entire area of laryngeal and perilaryngeal tissues accessible, and doubtless some good effect is due to systemic absorption as well as to the local action. Other iodin preparations are Lugol's solution, compound tincture of iodin, arsenic iodid, iron iodid, and metallic iodin encapsulated with some fatty or mucilaginous vehicle or emulsionized with cod-liver oil: all of which may be used under special conditions not necessary to detail here.

CREOSOTE GROUP.

The creosote group is large and contains a number of useful agents—carbolic acid, creosote, guaiacol, and combinations of creosote and guaiacol. I have not used carbolic acid for internal administration, though it

may sometimes be usefully employed locally, in proper dilution, and has been given hypodermically in sterilized olive-oil, in strength of from 1 to 10 per cent., and in doses of from 1 grain to 10 grains. The urine must be carefully watched when carbolic acid or creosote is used in this way. Beechwood creosote is a sufficiently good prepartion, provided a pure article can be obtained. Much of the commercial creosote contains impurities that irritate the stomach and the kidneys, but there are at least two good preparations in the market, and if care be exercised to obtain one of these the drug can be given in very large doses without untoward effect. Beginning with ½ minim three times daily, it is my custom to increase cautiously up to the point of tolerance, maintaining at that point or decreasing, according to the results in the individual case. I have given as much as 40 minims three times daily. An average dose is 10 minims three or four times daily. It may be given in milk, in which case two hours after meals is a very good time for its administration, as thereby the patient is induced to drink a glass of milk at that time. It may be shaken up with cod-liver oil and taken immediately after meals, or it may be made a part of a compound emulsion of cod-liver-oil. It should not be given in capsule unless associated with at least 5 minims of an oily vehicle to each minim of creosote. Capsules may thus be prepared with morrhuol or cod-liver oil as excipient. When creosote can not be taken by the stomach in sufficiently large doses. it may be given emulsionized with cod-liver oil or milk. by the rectum, and some have given it in sterilized olive-oil hypodermically. Creosote carbonate, commercially known as creosotal, is perhaps the best form in which to give creosote, as it rarely upsets digestion, the taste is not objected to, and in many cases it can be given in dram doses without untoward effect. Such doses may be persisted in for prolonged periods. I frequently give it in hot milk two hours after meals. though it may be given in water or without vehicle, if taken at meal time. The objection to it is its high cost. Recently creosote valerianate and other creosote combinations have been brought forward and are said to possess advantages over those mentioned. I have had as yet too little experience to speak positively concerning this.

Guaiacol, to which some attribute all the good effects of creosote, may be given in the liquid form, just as creosote is given; or its salts, which are tasteless powders, may be substituted. Of these, I prefer on the whole guaiacol carbonate, though in certain cases the benzoate and the salicylate seem to have advantages; the benzoate especially when there is a tendency to diminution of urine and the salicylate when high fever is a marked symptom. The dose is 10 to 60 grains daily, 20 grains being an average dose. Guaiacol potassium sulphonate is a recent addition to the list of combinations and is highly lauded by some writers. The objection to the guaiacol salts also is their cost. Their great advantage is the readiness with which they can be administered, and their lack of untoward local effect. Liquid guaiacol sometimes has seemed to be useful as an analgesic and antiphlogistic application topically in cases of laryngeal infiltration. As its pain-relieving effect is preceded by intense burning, the latter should be guarded against by a preliminary application of cocain, as in the case of other local agents. It is a useful ingredient in external applications to relieve pain; and slowly rubbed in drop by drop, in doses of 20 to 40 drops, the site of application being then covered with cotton and oiled silk, it may serve as a temporary expedient to reduce high temperature otherwise uncontrollable. One must guard against chill following this method.

BALSAMICS AND TEREBINTHINATES.

Another group of drugs useful in controlling morbid conditions, especially catarrhal processes, in the lungs and bronchi, in relieving cough, and in correcting the character of the expectorated matters, is formed by the balsamics and terebinthinates. Of these I would call special attention to myrtol, which may be given in doses of from 5 to 10 minims, dropped on sugar, encapsulated, or emulsionized, just as one would give turpentine, terebene, eucalyptol, or other agent of this group. For the production of results, its use must be persisted in for several weeks at least. Ichthyol also may be given internally in capsule, alone or combined with some of the drugs already mentioned, and seems to have especially good effect in the correction of collateral fetid bronchitis.

For the correction of local conditions in the throat, trachea, and bronchial passages, and in combating the septic processes of the tertiary stage, so much more destructive than tuberculosis in itself, as well as for sedative effect, drugs may be employed by inhalation or by intratracheal injection.

INHALANTS.

For inhalation, myrtol, eucalyptol, thymol, menthol, oil of peppermint, camphor, chloroform, bromoform, creosote, formaldehyde, and ethyl iodid may be used singly or variously combined. The little perforated zinc respirator, designed by Dr. Burney Yeo, is an extremely useful appliance for this purpose, and for continuous respiration by its aid combinations like the following may be used: chloroform, eucalyptol, creosote, alcohol, equal parts; myrtol, chloroform, terebene, equal parts, etc.

ETHYL IODID AND FORMALDEHYDE.

Among these drugs, however, I desire especially to signalize two, ethyl iodid and formaldehyde. The former may be used very simply by merely unstoppering the amber-colored, little-necked, ounce vial in which it should be kept. The heat of the hand is sufficient to volatilize the medicament. The vial may be held to the mouth or nostrils and deep breaths taken for from one to five minutes, according to the effect. This may be repeated as necessary; in cases of irritative cough, as often as every half hour. It is especially useful in cases of laryngeal tuberculosis. I have experimented in various ways to obtain formaldehyde in proper shape for inhalation. The little lamp, by means of which paraform is converted into formaldehyde gas, has seemed on the whole the best. This is allowed to impregnate the air of the room in which the patient remains, menthol or eucalyptol being sometimes volatilized concurrently; or, covering his eyes, the patient sits by the lamp and every now and then gathers in his incurvated palm some of the gas diluted with atmospheric air and inhales that: or paraform tablets may be crushed in the hand, and the endeavor made to get a certain amount of diluted gas from this. Or in a simple wash-bottle inhaler of 12-ounces capacity a solution of formaldehyde in water

may be added to glycerin and aromatics, the whole mixture making about 3 ounces. The strength of the formaldehyde solution is from 1 per cent. to 2 or 3 or even 5 per cent., as the patient bears it. None of these methods, and no other method that I have employed, is entirely satisfactory. If formaldehyde gas, properly diluted, could be collected in a reservoir and from this inhaled, as oxygen, nitrous oxid, and the like are inhaled, it would undoubtedly be useful.

PALLIATION OF FEVER.

In the course of the disease, whether toward recovery or death, there are a number of special symptoms and symptom-groups developed, for which palliative measures may be employed. Some of these may be referred to briefly. Fever, that is to say, temperature persisting at, or persistently recurring to, 100 F., or more, needs palliation, preferably by rest and the application of an ice-bag over the heart. And I may here interpolate that a long sea-voyage is the best possible treatment for patients exhibiting this tendency. The coal-tar products may be used cautiously if necessary to give the patient comfort; they are not curative of the conditions—the intoxication—causing the fever. Much better in many cases is the inhalation of nitrous oxid in the forenoon—i. e., before the expected rise of temperature—usually in two sittings, two hours apart; about 8 gallons mixed with atmospheric air, at each sitting. The mixture is obtained by inhaling pure nitrous oxid through the mouth, the nose being left uncovered. The ordinary cylinder and wash-bottle form the preferable apparatus. Oxygen inhalations are counterindicated.

TREATMENT OF HEMORRHAGE.

Hemorrhage, an alarming accident to the patient, the family and the inexperienced physician, will subside spontaneously in nine cases out of ten, if the patient be put at rest. Cold applications are generally useful, an ice-bag being applied over the heart, or over the seat of bleeding, if that can be located without undue disturbance to the patient. Cold food only is to be given, and in small quantities. Use of the voice is to be interdicted, and laxatives should be given to prevent straining at stool. When necessary, the force of the heart's action

can be reduced by aconite in appropriate doses, and cough be checked by opium, codein, or morphin. It is possible that heroin may serve better than the natural morphin. In severe cases, morphin may be given hypodermically up to the point of tolerance. The most generally useful drug to promote coagulation of blood and the formation of permanent clot, sealing the wound in the vessel or vessels, is crystallized calcium chlorid. With this, codein, turpentine, or thymus extract may be associated. The calcium salt is to be given in dilute solution in comparatively large doses, say 15 grains every second hour, for not more than four days consecutively. If medication is still necessary, lead acetate may then be given—say 3 or 5 grains in pill with an equal quantity of tannic acid and perhaps a grain of opium, three or four times daily. After two or three days, aromatic sulphuric acid should then be given, after which, if necessary, the calcium salt may be resumed. Ergot is useless in most cases. Atropin sulphate, say 1/120 grain, given hypodermically at the beginning of hemorrhage will often cut it short. Hydrastinin hydrochlorate is among the useful astringents.

NIGHT-SWEATING.

For night-sweating, agaracin, hyoscin hydrobromate, potassium tellurate, camphoric acid, atropin, strychnin, picrotoxin, and the like, are useful internally, while sponging with alcohol and alum, or with an alcoholic solution of quinin, or dusting with zinc oxid or zinc oleostearate will sometimes render internal medication unnecessary.

DIARRHEA.

Diarrhea is often exceedingly troublesome and not to be controlled by regulation of diet. Among the drugs useful in different cases are arsenic, mercuric chlorid, cupric sulphate, iron sulphate, tincture of ferric chlorid, opium, tannic and gallic acids, bismuth salicylate, benzonaphthol, salol, guaiacol salts, etc. Before using either astringents or opium, the bowel should be thoroughly washed out by the administration of calomel in small doses, followed by a saline laxative, and this by irrigation with hot—physiologic—saline solution. Notwithstanding, however, the combined use of astringents, opiates

and antiseptics, this symptom proves rebellious in many cases.

CONCLUSION.

The object of this paper, however, has not been to go into details of treatment or to advocate the use of any special agent in any special condition; above all, not to seem to prefer drugs to the hygienic and nutritional measures already sufficiently alluded to, and of which may again be specified open-air life with abundance of sunlight, as the most important of all. I have wished simply to indicate for what purposes drugs may wisely be employed, and to suggest different groups of agents applicable for these purposes, from which choice is to be made according to all the circumstances of the particular patient, time and place. Bearing in mind the limitations of drugs as well as their powers, and carefully selecting them for definite purposes, they may thus be made to fulfil their useful, but secondary part in the treatment of patients having pulmonary tuberculosis.